Procedural Results and Clinical Outcomes of Transcatheter Aortic Valve Implantation in Switzerland: An Observational Cohort Study of Sapien 3 Versus Sapien XT Transcatheter Heart Valves

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Abstract: BACKGROUND New generation transcatheter heart valves (THV) may improve clinical outcomes of transcatheter aortic valve implantation. METHODS AND RESULTS In a nationwide, prospective, multicenter cohort study (Swiss Transcatheter Aortic Valve Implantation Registry, NCT01368250), outcomes of consecutive transfemoral transcatheter aortic valve implantation patients treated with the Sapien 3 THV (S3) versus the Sapien XT THV (XT) were investigated. An overall of 153 consecutive S3 patients were compared with 445 consecutive XT patients. Postprocedural mean transprosthetic gradient (6.5±3.0 versus 7.8±6.3 mm Hg, P=0.17) did not differ between S3 and XT patients, respectively. The rate of more than mild paravalvular regurgitation (1.3% versus 5.3%, P=0.04) and of vascular (5.3% versus 16.9%, P<0.01) complications were significantly lower in S3 patients. A higher rate of new permanent pacemaker implantations was observed in patients receiving the S3 valve (17.0% versus 11.0%, P=0.01). There were no significant differences for disabling stroke (S3 1.3% versus XT 3.1%, P=0.29) and all-cause mortality (S3 3.3% versus XT 4.5%, P=0.27). CONCLUSIONS The use of the new generation S3 balloon-expandable THV reduced the risk of more than mild paravalvular regurgitation and vascular complications but was associated with an increased permanent pacemaker rate compared with the XT. Transcatheter aortic valve implantation using the newest generation balloon-expandable THV is associated with a low risk of stroke and favorable clinical outcomes. CLINICAL TRIAL REGISTRATION URL: http://www.clinicaltrials.gov. Unique identifier: NCT01368250.

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Procedural Results and Clinical Outcomes of Transcatheter Aortic Valve Implantation in Switzerland

An Observational Cohort Study of Sapien 3 Versus Sapien XT Transcatheter Heart Valves

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Background—New generation transcatheter heart valves (THV) may improve clinical outcomes of transcatheter aortic valve implantation.

Methods and Results—In a nationwide, prospective, multicenter cohort study (Swiss Transcatheter Aortic Valve Implantation Registry, NCT01368250), outcomes of consecutive transfemoral transcatheter aortic valve implantation patients treated with the Sapien 3 THV (S3) versus the Sapien XT THV (XT) were investigated. An overall of 153 consecutive S3 patients were compared with 445 consecutive XT patients. Postprocedural mean transprosthetic gradient (6.5±3.0 versus 7.8±6.3 mm Hg, P=0.17) did not differ between S3 and XT patients, respectively. The rate of more than mild paravalvular regurgitation (1.3% versus 5.3%, P=0.04) and of vascular (5.3% versus 16.9%, P<0.01) complications were significantly lower in S3 patients. A higher rate of new permanent pacemaker implantations was observed in patients receiving the S3 valve (17.0% versus 11.0%, P=0.01). There were no significant differences for disabling stroke (S3 1.3% versus XT 3.1%, P=0.29) and all-cause mortality (S3 3.3% versus XT 4.5%, P=0.27).

Conclusions—The use of the new generation S3 balloon-expandable THV reduced the risk of more than mild paravalvular regurgitation and vascular complications but was associated with an increased permanent pacemaker rate compared with the XT. Transcatheter aortic valve implantation using the newest generation balloon-expandable THV is associated with a low risk of stroke and favorable clinical outcomes.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01368250.

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Key Words: aortic valve stenosis ■ bleeding ■ transcatheter aortic valve replacement ■ transcatheter heart valve ■ transcutaneous aortic valve implantation ■ vascular complications

Since the first transcatheter aortic valve implantation[1] (TAVI) in 2002 and the establishment of the retrograde transfemoral approach[2] in 2005, the procedure has undergone further refinements.[3] Lower profile delivery systems,[4] multimodality imaging for patient screening[5] and device deployment,[6] transcatheter heart valve (THV) sizing algorithms,[7] and modifications of prosthesis design[8] and delivery systems have reduced the rate of vascular complications[4] and paravalvular regurgitation[7] (PAR) and increased the safety and efficacy of TAVI.[9,10] Although the procedure was initially restricted to inoperable patients,[11] it is currently approved for operable patients at high surgical risk.[12] Recently, a randomized trial[13]

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A list of collaborators and Swiss TAVI Investigators is available in the Data Supplement.

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WHAT IS KNOWN

- Transcatheter aortic valve implantation (TAVI) with the Sapien XT transcatheter heart valve (THV) is a valuable alternative to surgical aortic valve replacement in selected patients.
- However, TAVI is associated with vascular and bleeding complications, paravalvular regurgitation, and atrioventricular conduction disturbances.

WHAT THE STUDY ADDS

- In this preliminary comparison, the use of the new generation Sapien 3 THV was associated with a lower incidence of vascular complications and less paravalvular regurgitation compared with TAVI with the Sapien XT THV.
- The rate of new pacemaker implantation was higher after TAVI with the Sapien 3 THV than after TAVI with the Sapien XT THV.

has indicated superiority of TAVI over surgical aortic valve replacement for 1-year survival in patients with symptomatic severe aortic stenosis and a mean Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) of 7.3±3.0%, indicating intermediate surgical risk.

In 2014, the newest generation balloon-expandable THV[14] (Sapien 3, S3; Figure 1) received regulatory approval and was introduced in Switzerland and subsequently replaced its predecessor the Sapien XT (XT; Figure 2) THV as the default balloon-expandable THV for TAVI. The S3 may be delivered via a lower profile delivery system and incorporates a sealing cuff intended to reduce PAR. Despite positive results during the first-in-human S3 experience[14] and subsequent small[15,16] series, it is not established whether the new features of the S3 will translate into improved procedural and clinical outcomes compared with the XT. We therefore analyzed and compared all patients who underwent transfemoral TAVI with the S3 or the XT in the prospective, nationwide Swiss TAVI registry in Switzerland (ClinicalTrials.gov NCT01368250).

Methods

The Swiss TAVI registry is—as previously described[17]—a national, prospective cohort study of all TAVI procedures performed in Switzerland aiming for consecutive patient enrollment and with data monitoring as well as end point adjudication by a dedicated clinical events committee according to the recommendations of the Valve Academic Research Consortium.[18] The Swiss TAVI registry was designed to provide short-term clinical outcomes and long-term clinical data of TAVI patients treated with CE-approved devices. The study protocol was approved by the local cantonal ethics committee and institutional review boards at each participating center, and all patients provided written informed consent. The Swiss TAVI registry is performed under the lead of the Swiss Cardiovascular Center Bern at Bern University Hospital in cooperation with the Clinical Trials Unit Bern responsible for data management and independent statistical analysis.

For this analysis, all patients of the Swiss TAVI registry who underwent transfemoral TAVI with either the XT or the S3 THV were analyzed (inclusion period: XT, February 2011 to January 2014; S3, February 2014 to June 2014). The grade of PAR was assessed by transthoracic echocardiography before hospital discharge by highly experienced echocardiographers according to Valve Academic Research Consortium-2 guidelines.[18] Prespecified end points were more than mild PAR, vascular complications, major bleeding, new permanent pacemaker implantation (PPM), disabling stroke, and mortality after 30-day of follow-up.

Statistical Analysis

Continuous data are reported as mean±standard deviation (SD), and categorical variables are reported as number of patients (% of patients). Events are reported as counts of first occurrence per (sub) type of event (% of all patients). Event probabilities at 30 days were compared for patients treated with the XT versus the S3 bioprosthesis using logistic regressions. Reported are crude odds ratios (with 95% confidence intervals) with P values from Wald χ^2 tests corrected for random effects of the hospital identifier using mixed effects logistic regressions or exact logistic regression odds ratios with P values from exact tests in case of zero events. Reported are adjusted odds ratio (95% confidence interval), with the 2 valves compared using mixed effects logistic regressions, including (1) adjustment for TAVI procedure date (ie, to account for a potential learning effect of time), (2) random effect of hospital identifier, and (3) adjustment for baseline characteristics using inverse probability of treatment weights (ie, to account for potential disbalances between the 2 valve types concerning the patient population treated). The estimates of adjusted odds ratio from 20 data sets after multiple imputation of missing values were combined using Rubin's rule and presented with adjusted P values (P_{adj}). Inverse probability of treatment weights for S3 versus XT THV was calculated within each of the 20 data sets using the following baseline variables: age, sex, body mass index, diabetes mellitus, dyslipidemia, hypertension, previous pacemaker, history of myocardial infarction, cardiac surgery, cerebrovascular event, peripheral vascular disease, chronic obstructive pulmonary disease, coronary artery disease, left ventricular ejection fraction, aortic valve area, mean aortic valve gradient, moderate or severe mitral regurgitation, New York Heart Association class III or IV, Canadian Cardiovascular Society angina class none or I/II or III/IV, logistic EuroSCORE, STS PROM score, and valve size. No adjusted analyses were performed

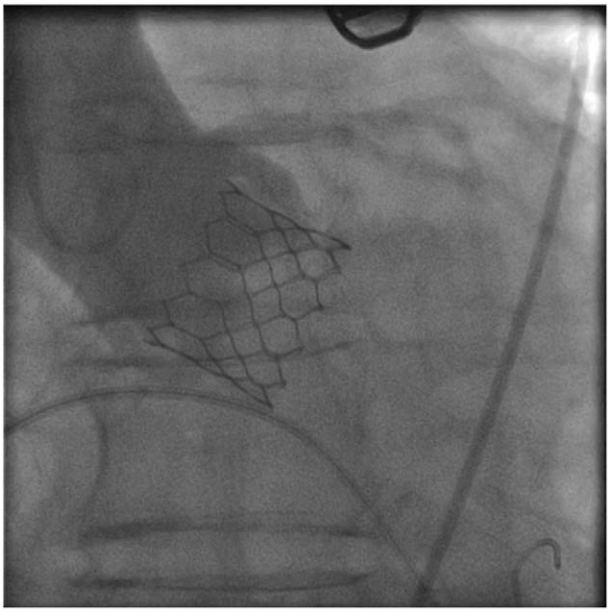

Figure 1. Aortic root angiogram after Sapien 3 transcatheter heart valve implantation. The Sapien 3 transcatheter heart valve comprises a balloon expandable, cobalt chromium frame, a trileaflet bovine pericardial tissue valve, and a polyethylene terephthalate (PET) skirt. The outer PET cuff was designed to improve paravalvular sealing.

Figure 2. Aortic root angiogram after Sapien XT transcatheter heart valve implantation. The Sapien XT transcatheter heart valve is approved for the treatment of symptomatic severe aortic stenosis in patients at high or prohibitive surgical risk. It comprises a balloon-expandable cobalt chromium frame, a trileaflet bovine pericardial tissue valve, and a polyethylene terephthalate inner skirt.

for outcomes with <10 events overall. Two-sided *P* values <0.05 were considered statistically significant. All analyses were performed with Stata version 14 (StataCorp, College Station, TX).

Results

Overall, 153 consecutive S3 patients and 445 consecutive XT patients were included in this study. The cohort represents consecutive all-comers with symptomatic severe aortic stenosis undergoing transfemoral TAVI with a balloon-expandable THV in Switzerland. Baseline characteristics are shown in Table 1. Except for dyslipidemia, which was more prevalent in patients receiving the XT THV, there were no significant differences in baseline characteristics. Importantly, no significant differences were found for age (82.2±6.1 versus 82.2±6.8 years, *P*=0.94), STS PROM (7.2±6.5% versus 8.5±7.9%, *P*=0.07), and preprocedural mean aortic valve gradient (47.2±22.0 versus 43.7±17.3 mm Hg, *P*=0.06) between S3 and XT patients, respectively.

Some procedural characteristics changed during the course of the trial (Table 2). Because of the establishment of hybrid operating rooms, more S3 patients were treated in this setting (S3 32.7% versus XT 22.9%, *P*=0.02) compared with XT patients who were mostly treated in cardiac catheterization laboratories (S3 66.7% versus XT 77.1%, *P*=0.01). Although procedural time did not change, there was less contrast dye used in S3 patients (S3 158.0±87.4 versus XT 201.2±95.4 mL, *P*<0.01), and there appeared a trend to perform the procedure without the use of general anesthesia in S3 patients (S3 69.9% versus XT 61.3%, *P*=0.06). Postprocedural mean transprosthetic gradient (6.5±3.0 versus 7.8±6.3 mm Hg, *P*=0.17) did not differ between S3 and XT patients, respectively.

Significant differences in the occurrence of PAR (Figure 3) were observed between S3 and XT patients. In more than half of S3 patients, no PAR was detected (57.3%), although this was observed in only one third of XT patients (31.9%, *P*<0.01). Mild PAR was also less frequent in S3 compared with XT patients (S3 41.3% versus XT 62.9%, *P*<0.01). Furthermore, the rate of more than mild PAR was significantly lower in S3 compared with XT patients (S3 1.3% versus XT 5.3%, *P*=0.04).

At 30-day (Table 3) follow-up, mortality did not differ between S3 and XT patients (S3 3.3% versus XT 4.5%, *P*=0.52, P_{adj}=0.27). Major disabling stroke was low in both groups (S3 1.3% versus 3.1%, *P*=0.24, P_{adj}=0.29). The rate of PPM implantation was higher in S3 patients (S3 17.0% versus XT 11.0%, *P*=0.06, P_{adj}=0.01). Major bleeding occurred twice as often in XT patients than in S3 patients (S3 3.9% versus XT 8.3%, *P*=0.11, P_{adj}=0.81) albeit not significantly different, but the rate of vascular complications (major and minor) was significantly higher in XT patients (S3 5.2% versus XT 16.9%, *P*<0.01, P_{adj}<0.01).

Discussion

This study sought to investigate differences in procedural and clinical outcomes of patients undergoing transfemoral TAVI with the S3 versus the XT THV. Analysis of our nationwide, prospective Swiss TAVI registry showed that TAVI with the S3 significantly reduced PAR and vascular complications in comparison to TAVI with the XT.

The success of TAVI depends on the risk of perioperative complications, the predictability of the procedure, and device durability. Within the last decade, multimodality imaging for patient screening, patient selection, and device deployment and iterations to the bioprostheses and refinement of delivery systems have contributed to the successful global spread of TAVI as an alternative to surgical aortic valve replacement. Minimizing the rate of periprocedural complications is mandatory to broaden the indication of TAVI from prohibitive or high surgical risk to intermediate[13,19] and low surgical risk[19] patients. Considering the S3 as a step into this direction has to be based on firm scientific evidence. Important complications of TAVI that need to be reduced are stroke, PAR, vascular and bleeding complications, and atrioventricular block.

Paravalvular Regurgitation

PAR is frequently observed after TAVI[20] and is associated with worse survival in patients with moderate to severe PAR.[21] Whether mild PAR is an independent mortality predictor, as suggested by a previous study,[22] is a matter of controversy. Important predictors for PAR include severe leaflet, annulus and left ventricular outflow tract calcifications, THV undersizing, and THV malpositioning. New THV designs with peri-prosthetic sealing cuffs (eg, the S3) may contribute to a reduction in PAR. In our study, more than mild PAR was less frequently observed after TAVI with the S3 compared with the XT. This may be attributed to the external skirt of the S3. However, improved sizing algorithms and a broader landing zone of the elongated S3 stent frame may also have contributed to the difference. As more than mild PAR is associated with higher mortality,[21] this difference may translate into improved TAVI

Table 1. Baseline Characteristics

	Sapien 3, N=153	Sapien XT, N=445	*P* Value
Age, years	82.21±6.05	82.26±6.75	0.94
Female gender, n (%)	72 (47.1%)	249 (55.8%)	0.07
Body mass index, kg/m^2	26.90±5.56	26.75±4.95	0.75
Cardiac risk factors			
Diabetes mellitus, n (%)	39 (25.5%)	112 (25.1%)	0.92
Dyslipidemia, n (%)	65 (42.5%)	236 (52.9%)	0.03
Hypertension, n (%)	117 (76.5%)	353 (79.1%)	0.49
Past medical history			
Previous pacemaker implantation, n (%)	15 (9.8%)	35 (7.8%)	0.49
Previous myocardial infarction, n (%)	24 (15.7%)	67 (15.0%)	0.89
Previous cardiac surgery, n (%)	17 (11.1%)	59 (13.2%)	0.57
Previous cerebrovascular accident, n (%)	20 (13.1%)	51 (11.4%)	0.56
Clinical features			
Peripheral vascular disease, n (%)	24 (15.7%)	65 (14.6%)	0.79
Chronic obstructive pulmonary disease, n (%)	22 (14.4%)	52 (11.7%)	0.39
Coronary artery disease, n (%)	86 (56.2%)	242 (54.3%)	0.71
Left ventricular ejection fraction, %	56.66±14.67	56.26±13.51	0.78
Aortic valve area, cm^2	0.71±0.23	0.71±0.22	0.88
Mean transaortic gradient, mm Hg	47.18±22.04	43.74±17.27	0.06
Mitral regurgitation grade moderate or severe	21 (14.2%)	86 (20.5%)	0.11
New York Heart Association (NYHA) Class			
NYHA I or II, n (%)	48 (32.9%)	150 (33.7%)	0.92
NYHA III or IV, n (%)	98 (67.1%)	295 (66.3%)	0.92
Canadian Cardiovascular Society Angina Class	n=152,	n=446,	0.15
No angina, n (%)	125 (82.2%)	333 (74.7%)	0.06
CCS I or II, n (%)	19 (12.5%)	75 (16.8%)	0.25
CCS III or IV, n (%)	8 (5.3%)	38 (8.5%)	0.22
Risk assessment			
Log. EuroScore, %	23.71±15.95	21.01±15.99	0.16
STS score, %	7.15±6.50	8.52±7.98	0.07

Dyslipidemia was more prevalent in the Sapien XT group. All other baseline characteristics did not differ significantly between groups. CCS indicates Canadian Cardiovascular Society; and STS, Society of Thoracic Surgeons.

outcomes. However, as the rate of more than mild PAR was low in our cohort, it did not impact short-term survival.

Stroke

Compared with medical management, TAVI is associated with an increased stroke risk.[11] Furthermore, in the Placement of Aortic Transcatheter Valve (PARTNER) trial, patients undergoing TAVI had a higher 30-day rate of any cerebrovascular event compared with patients randomized to surgical aortic valve replacement.[12] However, this difference disappeared at 2-year follow-up.[22] Subsequent studies with newer generation devices and large registries have further calmed the debate about TAVI associated stroke risk.[9] In the French Aortic National CoreValve and Edwards Registry (FRANCE II) study,[23] stroke rates were 2.3%, and in the United Kingdom Transcatheter Aortic Valve Implantation (UK TAVI) registry,[24] the rate was 4.1%. In our study, the 30-day disabling stroke rate with the S3 in an all-comer population was as low as 1.3%, which was numerically lower than that for the XT. If and how the incidence of stroke can be further reduced is a matter of debate. Cerebral protection devices[25] were designed to capture or deflect debris during TAVI, which would have otherwise embolized to the brain. However, there is currently no evidence that supports the routine use of these devices.[26] The clinical significance of a reduction in subclinical lesions on brain scanning post TAVI, which has been shown with the Claret device (Claret Embolic Protection and TAVI [CLEAN-TAVI] trial, NCT01833052, presented at Transcatheter Cardiovascular Therapeutics Congress 2014), was not established. Future clinical trials are needed to prove whether these devices effectively reduce the risk of stroke during TAVI. In our study population, a cerebral protection device was rarely used and not documented in the files.

Vascular Complications

Major vascular complications during TAVI are independent predictors of mortality.[27] With the first generation balloon-expandable THV, major vascular complications occurred in

Table 2. Procedural Characteristics

	Sapien 3, N=153	Sapien XT, N=445	*P* Value
Procedure time, min	71.72±30.54	71.80±27.98	0.98
Amount of contrast, mL	158.04±87.39	201.18±95.37	<0.01
General anesthesia, n (%)	46 (30.1%)	172 (38.7%)	0.06
Lenght of hospital stay, days	9.07±5.72	9.52±5.31	0.38
Type of access			0.82
Percutaneous, n (%)	133 (86.9%)	390 (87.6%)	0.89
Surgical, n (%)	20 (13.1%)	55 (12.4%)	0.89
Procedure location			
Catheterization laboratory, n (%)	102 (66.7%)	343 (77.1%)	0.01
Operating room, n (%)	1 (0.7%)	0 (0.0%)	0.26
Hybrid room, n (%)	50 (32.7%)	102 (22.9%)	0.02
Concomitant procedure			
Percutaneous coronary intervention, n (%)	8 (5.3%)	45 (10.1%)	0.07
Carotid stenting, n (%)	0 (0.0%)	1 (0.2%)	1.00
Iliofemoral stenting, n (%)	5 (3.3%)	17 (3.8%)	1.00
Device features			
Valve size			
23 mm	42 (27.5%)	108 (24.3%)	0.45
26 mm	72 (47.1%)	257 (57.8%)	0.02
29 mm	39 (25.5%)	80 (18.0%)	0.05
Prior balloon aortic valvuloplasty, n (%)	143 (93.5%)	410 (92.1%)	0.72
Device features			
Mean transprosthetic gradient, mm Hg			
For 23 mm valve size	11.65±5.98	9.96±4.77	0.08
For 26 mm valve size	9.00±3.66	8.18±5.61	0.25
For 29 mm valve size	8.49±3.42	7.42±4.59	0.23
Aortic valve area, mm			
For 23 mm valve size	1.43±0.33	1.51±0.43	0.38
For 26 mm valve size	1.73±0.37	1.89±0.58	0.09
For 29 mm valve size	1.93±0.50	2.24±0.81	0.15
Aortic regurgitation post-TAVI	n=150	n=439	
Grade 0, n (%)	86 (57.3%)	140 (31.9%)	<0.01
Grade 1, n (%)	62 (41.3%)	276 (62.9%)	<0.01
Grade 2, n (%)	2 (1.3%)	20 (4.6%)	0.08
Grade 3, n (%)	0 (0.0%)	3 (0.7%)	0.57

16.2% of patients in the PARTNER IB trial.[11] Meanwhile, downsizing of access sheath diameters[4] allowing fully percutaneous procedures[28] has resulted in decreased vascular complications. In our study, major and minor vascular complications were significantly lower in S3 compared with XT patients. This parallels a study that showed decreased vascular complications with lower-profile compared with large-profile sheaths.[4] On a large scale, the reduction of major vascular complications with the S3 delivery system is expected to impact prognosis and speed up postprocedural patient mobilization, allowing earlier ambulation and discharge.

Bleeding

Major bleeding and blood transfusions after TAVI are associated with worse prognosis.[29,30] The source of bleeding may be procedure-related (eg, access site, ventricular or aortic perforation) or technically unrelated to TAVI but triggered by periprocedural antithrombotic medication (eg, gastrointestinal). The access site is the most common source of procedure-related bleeding. In this study, major bleeding occurred twice as often in patients receiving the XT than in patients treated with the S3 THV; however, the difference did not reach statistical significance. A lower rate of bleeding with the S3 may be attributed to the lower profile of the introducer sheath and delivery system. This observation parallels a study that compared TAVI outcomes with different sheath sizes[4] and may translate into improved outcomes.

Permanent Pacemaker Implantation

Atrioventricular conduction disturbances necessitating PPM implantation are frequently observed after TAVI[11] and

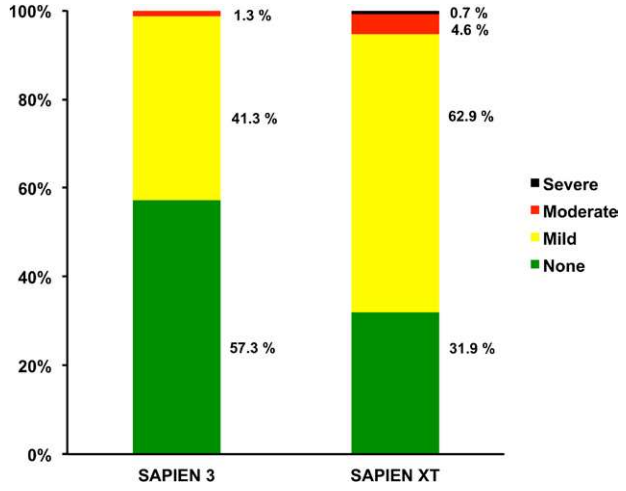

Figure 3. Paravalvular regurgitation after transcatheter aortic valve implantation with the Sapien 3 versus the Sapien XT transcatheter heart valve. Mild as well as more than mild paravalvular regurgitation was less frequently observed after implantation of the Sapien 3 compared with the Sapien XT transcatheter heart valve.

mostly depend on the THV type implanted. Although PPM rates of 20% to 30% with the self-expanding CoreValve[13,31] and almost 30% with the Lotus THV[32] have been observed, the rate of higher degree atrioventricular block is lower for balloon-expandable THVs.[33] Additional factors that predict PPM implantation after TAVI include preexisting right bundle branch block[34] or atrioventricular block, as well as THV implant depth[35] and annulus oversizing.[34] In our study, there were more new PPM implants in patients treated with the S3. This could be explained by the longer stent frame of the S3, which may protrude more into the left ventricular outflow tract, thereby compressing the interventicular septum. An inflammatory response to the external sealing skirt may be postulated, but is unlikely. Whether prudent higher THV implantations (80% aortal, 20% ventricular) may reduce the risk of conduction disturbances needs further investigation. Although the initial manufacturer recommendation was to place the middle marker of the deployment balloon in the annular plane, current clinical practice demonstrates that a high implant in experienced hands can be safely performed and may reduce atrioventricular conduction dusturbances.[36] Overall, there seems to be no prognostic impact of a new PPM after TAVI.[34,37]

Limitations

The grade of PAR in this study was defined by experienced onsite echocardiographers and reported according to Valve Academic Research Consortium-2 criteria.[18] The grading of PAR

Table 3. 30-Days Clinical Outcomes

	Sapien 3, N=153	Sapien XT, N=445	Odds Ratio OR (95% CI)	*P* Value	Adjusted OR (95% CI)	Adjusted *P* Value
Mortality, n(%)	5 (3.3)	20 (4.5)	0.72 (0.26–1.95)	0.56	0.63 (0.27–1.43)	0.27
Cardiovascular mortality, n (%)	4 (2.6)	19 (4.3)	0.60 (0.20–1.80)	0.36	0.77 (0.32–1.81)	0.55
Cerebrovascular accident, n (%)	2 (1.3)	18 (4.0)	0.31 (0.07–1.37)	0.12	0.35 (0.10–1.15)	0.08
Disabling stroke, n (%)	2 (1.3)	14 (3.1)	0.41 (0.09–1.81)	0.24	0.44 (0.10–1.99)	0.29
Nondisabling stroke, n (%)	0 (0.0)	2 (0.4)	1.20 (0.03–15.51)	1.00		
TIA, n (%)	0 (0.0)	2 (0.4)	1.20 (0.03–15.51)	1.00		
Myocardial infarction, n (%)	2 (1.3)	0 (0.0)	7.06 (0.55-∞)	0.13		
Periprocedural myocardial infarction, n (%)	2 (1.3)	0 (0.0)	7.06 (0.55-∞)	0.13		
Spontaneous myocardial infarction, n (%)	0 (0.0)	0 (0.0)				
Acute kidney injury, n (%)	7 (4.6)	26 (5.8)	0.83 (0.35–1.98)	0.89	1.62 (0.54–4.86)	0.39
Stage 1, n (%)	1 (0.7)	13 (2.9)	0.26 (0.03–2.08)	0.21	0.80 (0.18–3.58)	0.77
Stage 2, n (%)	2 (1.3)	3 (0.7)	1.95 (0.32–11.79)	0.47		
Stage 3, n (%)	4 (2.6)	10 (2.2)	1.17 (0.36–3.78)	0.80	2.79 (0.56–13.94)	0.21
Bleeding, n (%)	14 (9.2)	66 (14.8)	0.50 (0.26–0.99)	0.05	0.76 (0.24–2.40)	0.64
Life threatening bleeding, n (%)	6 (3.9)	24 (5.4)	0.64 (0.24–1.68)	0.36	1.16 (0.56–2.40)	0.68
Major bleeding, n (%)	6 (3.9)	37 (8.3)	0.48 (0.19–1.18)	0.11	0.84 (0.21–3.45)	0.81
Minor bleeding, n (%)	2 (1.3)	5 (1.1)	0.93 (0.13–6.59)	0.71		
Vascular access site and access-related complications, n (%)	8 (5.2)	75 (16.9)	0.25 (0.11–0.57)	<0.01	0.31 (0.17–0.59)	<0.01
Major vascular complications, n (%)	5 (3.3)	41 (9.2)	0.31 (0.11–0.85)	0.02	0.53 (0.27–1.04)	0.07
Minor vascular complications, n (%)	2 (1.3)	34 (7.6)	0.16 (0.03–0.74)	0.02	0.09 (0.04–0.19)	<0.01
Repeat unplanned intervention, n (%)	2 (1.3)	2 (0.4)	2.93 (0.41–21.01)	0.28		
Valve in valve treatment, n (%)	0 (0.0)	1 (0.2)	2.91 (0.00–113.43)	1.00		
Permanent pacemaker implantation, n (%)	26 (17.0)	49 (11.0)	1.68 (0.99–2.84)	0.06	1.89 (1.16–3.08)	0.01

Depicted are number of first events with % of all patients at 30 days since procedure. Odds ratios (OR) from mixed effects logistic regressions accounting for random hospital identifier effects or exact logistic regressions in case of zero events (95% confidence interval [CI]). Adjusted odds ratios: see Methods for details. TIA indicates transient ischemic attack.

after TAVI may be difficult and substantial inter- and intraobserver variability may occur. The lack of a core laboratory may lead to heterogeneity in the assessment of this parameter. However, all sites contributed patients to both groups, which reduces center-specific assessments as a confounder, and outcome assessments were corrected using random effects of the site.

As the S3 replaced the XT as default balloon-expandable THV, both groups were treated consecutively. A learning curve may be postulated explaining improved outcomes with the S3. However, all participating centers have started and gained extensive experience with TAVI before the SWISS TAVI registry was initiated. Furthermore, the introduction of a new device implicated a new learning curve for the S3, which would be in favor of the XT. Therefore, we do not anticipate that a learning curve explains the observations of this trial.

Assessments of clinical outcomes were not corrected for multiple testing, which may lead to the reporting of spurious significant effects. The reporting in this study followed the Valve Academic Research Consortium-2 criteria and were predefined. The reduction in vascular access site–related complications does withstand correction for multiple testing by the Bonferroni method (0.05 divided by 9 main outcomes: 0.005). Otherwise, further assessments of clinical outcomes comparing S3 versus XT is encouraged using a larger sample size of patients and longer follow-up. Because of the prospective design of this nationwide multicenter registry, data collection was restricted to variables defined at the launch of the registry. Therefore, no information on specific sizing algorithms and prosthesis implant depth are available.

Conclusions

The use of the new generation S3 balloon-expandable THV is associated with a significant reduction of more than mild PAR and vascular complications when compared with the XT. In contemporary clinical practice, TAVI using the newest generation balloon-expandable THV is associated with a low risk of stroke and overall favorable clinical outcomes.

Disclosures

Dr Binder serves as consultant to Edwards Lifesciences and proctor to Boston Scientific. Dr Jeger serves as a consultant to St Jude Medical and has received reimbursement for travel expenses from Medtronic, Boston Scientific, and Edwards Lifesciences. Dr Tueller received speakers fees from Edwards Lifesciences and travel expenses from Medtronic. Dr Toggweiler received speaker fees from Edwards Lifesciences and Medtronic. Dr Ferrari is a proctor for Edwards Lifesciences. Dr Noble serves as consultant for Medtronic. Dr Roffi received institutional research grants from Abbott Vascular, Boston Scientific, Biotronik, Biosensor, and Medtronic. Dr Jüni is an unpaid steering committee or statistical executive committee member of trials funded by Abbott Vascular, Biosensors, Medtronic, and Johnson & Johnson. CTU Bern, which is part of the University of Bern, has a staff policy of not accepting honoraria or consultancy fees. However, CTU Bern is involved in design, conduct, or analysis of clinical studies funded by Abbott Vascular, Ablynx, Amgen, AstraZeneca, Biosensors, Biotronic, Boehringer Ingelheim, Eisai, Eli Lilly, Exelixis, Geron, Gilead Sciences, Nestlé, Novartis, Novo Nordisc, Padma, Roche, Schering-Plough, St. Jude Medical, and Swiss Cardio Technologies. Dr Nietlispach serves as consultant to Edwards Lifesciences and St Jude Medical. Dr Huber is a proctor for Edwards Lifesciences and Consultant for Medtronic. Dr Windecker has received research contracts to the institution from Abbott, Boston Scientific, Biosensors, Cordis, Medtronic, and St Jude. Dr Wenaweser serves as proctor for Medtronic, Edwards Lifesciences, and Boston Scientific and has received an unrestricted grant from Medtronic to the institution (University of Bern). All the other authors have no conflicts of interest to declare.

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Supplemental Material

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Procedural Results and Clinical Outcomes of Transcatheter Aortic Valve Implantation in Switzerland: An Observational Cohort Study of Sapien 3 Versus Sapien XT Transcatheter Heart Valves

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